Sudden hearing loss following acute hepatitis

Ofer Yossepowitch, Alex Lossos, Izidore S Lossos

A 35-year-old previously healthy physician was admitted to the emergency room with a fever up to 40°C, extreme weakness and dark urine. The physical examination was remarkable for right upper quadrant abdominal tenderness and mild splenomegaly. He denied sore throat or direct contact with blood products. Laboratory studies disclosed elevated liver enzymes, hyperbilirubinaemia and bilirubinuria. A diagnosis of acute hepatitis was established. Initially, all serologic viral studies were negative. However, a late seroconversion for IgM to the early antigen (EA) of Epstein-Barr virus (EBV) in the presence of negative antibodies to Epstein-Barr nuclear antigen (EBNA), followed by a rise in the IgG titres to EA and EBNA were observed, indicating EBV to be the causative agent of the hepatitis. During follow-up examinations in our out-patient clinic, a gradual convalescence and normalisation of the abnormal liver function tests were observed.

Four weeks later the patient complained of a sudden hearing loss in his right ear which he had noticed subsequent to an examination of his patients with a stethoscope and after using a telephone handset with his right ear. He did not complain of tinnitus, nausea, vomiting or vertigo. The physical examination was normal, with a negative Romberg test and without nystagmus. A comprehensive audiologic assessment revealed a bilateral normal ear-drum with a normal pure-tone air and bone conduction (Weber and Rinne tests). The pure tone threshold analysis results are presented in figure 1. Treatment was initiated and the audiogram was repeated 10 days later (figure 2).

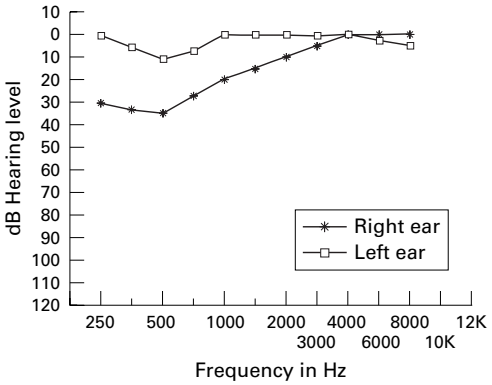

Figure 1 Audiogram performed on admission

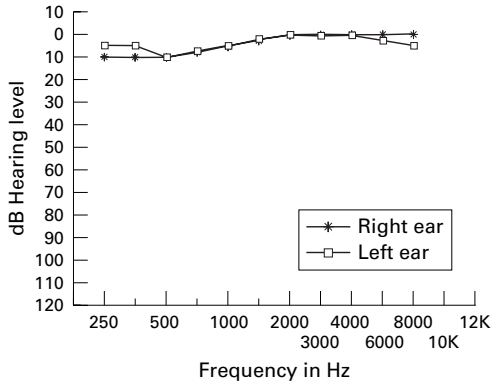

Figure 2 Audiogram performed 10 days after initiation of therapy

Hadassah University Hospital, Jerusalem, Israel
Department of Medicine
O Yossepowitch
I S Lossos
Department of Neurology
A Lossos

Correspondence to
Izidore S Lossos,
Department of Hematology,
Hadassah University
Hospital, POB 12000,
Jerusalem IL-91120, Israel

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Questions

1 What abnormality is demonstrated on the admission audiogram (figure 1) ?
2 What is the diagnosis and its cause ?
3 What are the possible additional common aetiologies of the presented disorder ?
4 Describe the changes in the audiogram presented in figure 2 compared to that in figure 1.

Answers

QUESTION 1
The audiogram performed on admission demonstrates a decrease of 20–35 dB hearing level at low to intermediate frequencies (250–1000 Hz) in the right ear. The left ear is normal.

QUESTION 2
The patient has a classic sudden sensorineural hearing loss following a preceding EBV infection. The performance-intensity function, including a speech reception threshold (SRT) analysis and a speech discrimination assay, resulted in a normal finding for the left ear, however, it was pathological for the right ear (SRT, right ear = 25 dB). A negative reflex decay with normal acoustic reflexes were observed. Computed tomography of the posterior fossa, an electronystagmogram, and auditory brainstem response testing were normal.

QUESTION 3
In the presented case, a preceding EBV infection yielded hearing loss by either gaining access to the inner ear, leading to several pathophysiologic changes, or causing an immune-mediated reaction, both resulting in the same impairment leading to sudden deafness. Additional common causes of sudden hearing loss include acoustic neuromas, Ménière's disease, ototoxic drugs and multiple sclerosis.

QUESTION 4
Following initiation of carbogen inhalations, prednisone and oxipurine treatment, the patient experienced a rapid improvement in auditory acuity. The repeated audiogram demonstrates complete recovery of the right ear hearing. No hearing disturbances were noticed during a 12-month follow-up.

Discussion

Sudden hearing loss (SHL) is a term generally used to refer to hearing loss of sensorineural origin evolving over a period of a few hours to a few days. Acoustic neuromas, Ménière's disease, multiple sclerosis and ototoxic drugs are among the most common causes. In some cases, the aetiology remains unknown. Idiopathic SHL has been reported to have an incidence of between 5 to 20 new cases per 100 000 population per year.[1] Several suggested theories attempt to elucidate the aetiopathogenesis of idiopathic SHL, including autoimmune diseases, a vascular insult and viral infections.

Several viruses have been strongly implicated as having a causative role in the pathogenesis of SHL. Veltri *et al*[2] and Wilson *et al*[3] studied the incidence of seroconversion to several viruses in a group of patients presenting with SHL compared with a healthy control group. In the SHL group of patients, there was a significantly higher incidence of seroconversion to mumps, rubella, rubeola, measles, herpes simplex, varicella-zoster, cytomegalovirus and influenza viruses types A & B. Moreover, in some patients with SHL, viruses were directly identified in the inner ear by either immunofluorescent methods[4] or perilymph cultures.[5]

EBV has only rarely been associated with SHL. The table summarises 14 reported cases of EBV infection complicated by hearing loss.[6–14] It usually occurs in young adults with infectious mononucleosis, their ages ranging between 7 and 58 years (mean, 21 years), with a considerable female predominance (M:F, 5:9). The hearing loss usually appears in the convalescent phase of the disease, but may infrequently be a presenting symptom.[12] The mean time between the acute illness to the appearance of hearing loss is 6 weeks, ranging from 2.5 weeks to 3.5 months (table). Both ears are equally vulnerable. The overall percentage of patients with bilateral SHL is 4–17%.[3] However, six out of the 14 (43%) cases of SHL attributed to EBV infection involved both sides (table). Audiometry analysis displays mild to severe impairment of intermediate or high frequencies. In rare cases, the spectrum of low frequencies is also involved.

EBV is an ubiquitous pathogen infecting most (>90%) of the world's population. It is associated with both benign disorders, such as infectious mononucleosis, and malignant disorders, such as Burkitt lymphoma and nasopharyngeal carcinoma. Less frequent manifestations include pneumonitis, cerebritis, mono- or polyneuritis, Guillian-Barre syndrome, myocarditis, pericarditis, thrombocytopenia, and agranulocytosis.[15]

Various neurologic manifestations have been associated with infectious mononucleosis, including Guillain-Barre syndrome, Bell's palsy, meningoencephalitis, and transverse myelitis.[16] These complications may occur in the absence of a clinically apparent infectious mononucleosis.

The exact mechanism leading to SHL following EBV infection has not been clearly determined. Schunknecht *et al*[17] studied the histopathology of temporal bones from SHL patients, and demonstrated atrophy of the organ of Corti, tectorial membrane, stria vascularis, cochlear nerve and vestibular organ. Identical pathologic findings were discovered in patients with established viral labyrinthitis. These authors suggested that viral particles gain access to the membranous cochlea by haematogenous spread (viraemia), replicate locally and lead to rapid pathophysiologic changes resulting in reduced blood flow to the inner ear that is frequently reversible but may be extremely destructive and result in permanent hearing loss.

Nevertheless, the scarcity with which EBV is associated with hearing loss, in addition to the significant attention that immune-mediated SHL has received, led Williams *et al*[13] to propose that, in certain susceptible individuals, a temporary cellular immunosuppression, which accompanies normal recovery from EBV infection, may provide an opportunity for reactivation of a viral agent already present in the inner ear. Thus, it appears that the role of EBV in sudden deafness has yet to be clarified.

The therapy currently advocated for SHL includes carbogen inhalations (a mixture of

Table Sudden hearing loss associated with EBV – clinical data

Ref	*Age (years), sex*	*Clinical manifestations of infectious mononucleosis*	*Lag period**	*Impaired frequencies***	*Side*	*Tinnitus*	*Additional neurologic signs*	*Outcome*
6	58, M	sore throat, cervical lymphadenopathy	8 weeks	N/R	right	–	Ataxia, diplopia, Guillain-Barre syndrome	Complete recovery
7	18, F	sore throat, malaise, high fever, cervical lymphadenopathy	2.5 weeks	60 dB loss at 2000 Hz	N/R	–	Mental confusion, memory loss, ataxia, bilateral papilloedema	Complete recovery
8	17, M	fatigue, anorexia, sore throat, high fever, cervical lymphadenopathy, hepatomegaly	2 weeks	100 dB loss at 4000 Hz	right	+	Vestibular nerve involvement	Slight recovery
9	20, F	high fever, lymphadenopathy	8 weeks	40 dB loss at 2000 Hz	left	–	Cranial neuropathy of V and VII, vertical nystagmus	Slight recovery
10	23, F	anorexia, autoimmune haemolytic anemia, acute hepatitis	6 weeks	60 dB loss at 6000 Hz	left	+	Tinitus	Slight recovery
11	25, F	fatigue, anorexia, sore throat, lymphadenopathy	N/R	25 dB loss at 8000 Hz	bilateral	–	None	Persistent
	32, F	anorexia, fatigue, lightheadedness, sore throat, cervical lymphadenopathy	N/R	35-dB loss at 8000 Hz	bilateral	–	None	Persistent
12	16, M	none	N/R	40 dB loss at 4000 Hz	bilateral	–	Ataxia, dysmetria, dysdiadochokinesia, dysarthria, bilateral nystagmus	Persistent
13	14, F	N/R	3.5 months	80 dB loss at 6000 Hz	bilateral	+	None	Persistent
	7, F	N/R	months	45-dB loss at 3000 Hz	bilateral	+	None	Persistent
	9, M	N/R	4 weeks	60-dB loss at 6000 Hz	left	+	None	Persistent
			5 months	80-dB loss at 500 Hz	right	+		
14	12, F	excessive tiredness	3 weeks	60 dB loss at 8000 Hz	bilateral	–	Seizures, acute psychotic reaction, acute encephalopathy	Persistent
	14, F	excessive tiredness, headache, exudative tonsilitis	4.5 weeks	80-dB loss at 2000 Hz	right	–	Dizziness	Persistent
Present case	35, M	high fever, malaise, acute hepatitis	4 weeks	35 dB loss at 500 Hz	right	–	None	Complete recovery

*The lag period is calculated from the time of infectious mononucleosis diagnosis to the notice of hearing loss.
**The specific frequency indicated in the table is the one most damaged within the range of frequencies found impaired at audiometry analysis.
N/R - Not reported.

95% oxygen and 5% carbon dioxide) in order to improve pO_2 levels in the perilymph[18] and systemic steroid therapy. The latter treatment is based on its anti-inflammatory effect in viral infections. It is noteworthy that no controlled studies have been performed with any of the suggested forms of therapy, which makes it difficult to judge whether a suggested therapy would result in a higher recovery rate than a spontaneous recovery.

Our review indicates a poor prognosis for the recovery of hearing in SHL following EBV infection. Of 14 reported cases, only three had complete recovery, three had slight recovery, and eight (57%) remained with permanent deafness (table). Generally, sudden deafness has a better prognosis than cases associated with EBV infection; one-third of patients have a return of normal hearing, one-third are left with a 40–80 dB speech reception threshold, and one-third have a total loss of useful hearing.[19] Spontaneous recovery of normal hearing is more likely to occur if the deafness is not associated with vertigo or advanced age. Once recovery of hearing begins, it is likely to take place very rapidly in a matter of a few days. The longer the delay between the onset of deafness and the onset of recovery, the worse the prognosis for complete recovery.[20] There is no difference in the outcome of patients in whom the hearing loss is isolated compared with those in whom hearing loss is associated with other neurologic complications (table). Although there are insufficient cases to yield a significant statistical conclusion, the data presented in the table suggest that, in the absence of tinnitus, the milder the intensity and the lower the impaired frequencies, the better is the likelihood of recovery.

Although SHL is rarely caused by EBV, physicians should be aware of this rare complication of EBV infection.

Final diagnosis

Sudden hearing loss associated with Epstein-Barr virus infection.

Keywords: hearing loss; Epstein-Barr virus.

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